We Claim:

A compound having the structure of Formula I,

Formula I

and its pharmaceutically acceptable salts, enantiomers, diastereomers, Novides, prodrugs, metabolites, polymorphs, pharmaceutically acceptable solvates,

wherein

Az is a five to seven membered heterocyclic ring having one to four

Formula I

heteroatoms selected from N, S, or O; the preferred heterocyclic ring is 1,2,4-triazol-1-yl;

Ar is a five to seven membered heterocyclic ring containing one to four heteroatoms selected from the group consisting of oxygen nitrogen and sulphur; phenyl or a substituted phenyl group having one to three substituents independently selected from halogen (e.g. chlorine, fluorine, bromine or iodine), nitro, cyano, lower(C_1 - C_4) alkyl, lower (C_1 - C_4) alkoxy or a perhalo lower (C_1 - C_4) alkyl, perhalo lower(C_1 - C_4) alkoxy; the preferred heterocyclic rings are thienyl and pyridyl;

R is H or methyl;

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R₁ is selected from the group consisting of

wherein

X is selected from the group consisting of CH2, O, S and SO2;

R₂ is hydrogen or lower(C₁-C₄) alkyl;

A is hydrogen, lower(C₁-C₄) alkyl, phenyl or phenyl substituted by one or more of groups independently selected from halogen (e.g. chlorine, fluorine, bromine or iodine atoms), nitro, cyano, hydroxy, lower(C₁-C₄) alkyl, lower (C₁-C₄) alkoxy or perhalo lower (C₁-C₄) alkyl, perhalo lower (C1-C4)alkoxy; substituted or unsubstituted five or six membered heterocyclyl ring systems containing one to four hetero atoms chosen from N. O and S, said heterocyclyl substituents being (C₁-C₈) alkanoyl, lower (C₁-C₄) alkyl, lower (C₁-C₄) alkoxy carbonyl, N, N-di(lower alkyl) amino carbonyl, aminothiocarbonyl, N-lower(C₁-C₄) alkyl (C_1-C_4) aminothiocarbonyl, N,N-di(lower alkyl) (C1-C4) aminothiocarbonyl, lower (C₁-C₄) alkyl sulfonyl, phenyl substituted lower (C₁-C₄) alkyl sulfonyl, N-lower (C₁-C₄) alkylamino, N, N-di(lower alkyl) (C₁-C₄) amino, 1,3imidazol-1-yl, 2-loweralkyl(C₁-C₄) sulfenyl-1,3-imidazol-1-yl, pyridinyl, thaizolyl, 1,2,4 triazol-4-yl or phenyl or phenyl substituted by one or more of groups independently selected from halogen (chlorine, fluorine, bromine or iodine), perhalo lower(C₁-C₄) alkyl, (C₂-C₈) alkanoyl, lower(C₁-C₄) alkyl, lower(C₁-C₄) alkyl substituted by one or more hydroxy group, lower(C₁-C₄)

alkoxy, nitro, cyano, hydroxy, 1,2,4-triazolyl, 1,3-imidazolyl, 1,2,3,4-tetrazolyl.

2. The compound of claim 1 having the structure of the Formula II

Formula II

(Formula I, wherein Az is 1,2,4-triazol -1-lyl; R is H or CH_3 ; Ar is 2, 4-dihalo substituted phenyl, Hal is Cl, F, Br or I; and R_1 is

wherein A is the same as defined in claim 1.

3. The compound of claim 2 having the structure of Formula II, wherein A is represented by

$$-\sqrt{N-z}$$

Z is a hydrogen, (C_1-C_8) alkanoyl, lower alkyl, (C_1-C_8) perhaloalkanoyl, or phenyl, phenyl substituted by one or more of groups independently selected from nitro, cyano, halogen (chlorine, fluorine bromine, iodine) perhalo lower (C_1-C_4) alkyl, perhalo lower (C_1-C_4) alkoxy; (C_2-C_8) alkanoyl, lower (C_1-C_4) alkyl, lower (C_1-C_4) alkyl substituted by one or more hydroxy

group, lower(C_1 - C_4) alkoxy, 1,3-imidazolyl, 1,2,4-triazolyl, 1,2,3,4-tetrazolyl, or OCH₂Y;

wherein Y is phenyl or phenyl substituted by one or more of groups independently selected from nitro, cyano, halo, perhalo lower alkyl, (C₂-C₈) alkanoyl lower alkyl, hydroxy, lower alkyl substituted by one or more hydroxy group, lower alkoxy, 1,3-imidazolyl, 1,2,4-triazolyl or 1,2,3,4-tetrazolyl.

4. A compound selected from the group consisting of:

2-[(5R,3R)-5-(2,4-Difluorophenyl)-tetrahydro-5-(1*H*-1,2,4-triazol-1yl-methyl)-furan-3-yl-methyl]-4-{4-[4-(phenyl)-1-piperazinyl]-chlorophenyl}-2,4-dihydro-3(2*H*,4*H*)-1,2,4-triazolone,

2-[(5R,3S)-5-(2,4-Difluorophenyl)-tetrahydro-5-(1*H*-1,2,4-triazol-1yl-methyl)-furan-3-yl-methyl]-4-[4-(phenyl)-1,2,4-triazol-1-yl]-2,4-dihydro-3(2*H*,4*H*)-1,2,4-triazolone,

2-[(5R,3S)-5-(2,4-Diflurophenyl)-tetrahydro-5-(1*H*-1,2,4-triazol-1yl-methyl)-furan-3-yl-methyl]-4-[4-(hydroxyphenyl)-2,4-dihydro-3(2*H*,4*H*)-1,2,4-triazolone,

2-[(5R,3R)-5-(2,4-Difluorophenyl)-tetrahydro-5-(1H-1,2,4-triazol-1yl-methyl)-furan-3-yl-methyl]-4-[4-(1,2,4-triazol-1-yl-methyl)-phenyl-2,4-dihydro-3(2H,4H)-1,2,4-triazolone,

2-[(5R,3S)-5-(2,4,Difluorophenyl)-tetrahydro-5-(1H-1,2,4-triazol-1yl-methyl)-furan-3-yl-methyl]-4-{4-[4-(phenyl)-1-piperazinyl]-chlorophenyl}-2,4-dihydro-3(2H,4H)-1,2,4-triazolone,

2-[(5R,3S)-5-(2,4-Difluorophenyl)-tetrahydro-5-(1H-1,2,4-triazol-1yl-methyl)-furan-3-yl-methyl]-4-[4-(benzyloxy)-phenyl]-2,4-dihydro-3(2H,4H)-1,2,4-triazolone,

2-[(5R,3S)-5-(2,4-Difluorophenyl)-tetrahydro-5-(1*H*-1,2,4-triazol-1yl-methyl)-furan-3-yl-methyl]-4-[4-[4-[4-(benzyloxy)-phenyl]-1-piperazinyl]-phenyl]-2,4-dihydro-3(2*H*,4*H*)-1,2,4-triazolone,

2-[(5R,3R)-5-(2,4-Difluorophenyl)-tetrahydro-5-(1*H*-1,2,4-triazol-1yl-methyl)-furan-3-yl-methyl]-4-[4-(2,2,3,3-tetrafluoropropoxy)-phenyl]-2,4-dihydro-3(2*H,4H*)-1,2,4-triazolone,

2-[(5R,3R)-5-(2,4-Difluorophenyl)-tetrahydro-5-(1*H*-1,2,4-triazol-1yl-methyl)-furan-3-yl-methyl]-4-[4-(1,2,3,4-tetrazol-1-yl)-phenyl]-2,4-dihydro-3(2*H*,4*H*)-1,2,4-triazolone,

2-[(5R,3S)-5-(2,4-Difluorophenyl)-tetrahydro-5-(1H-1,2,4-triazol-1yl-methyl)-furan-3-yl-methyl]-4-[4-(2,4-dichlorobenzyloxy)-phenyl]-2,4-dihydro-3(2H,4H)-1,2,4-triazolone,

2-[(5R,3R)-5-(2,4-Difluorophenyl)-tetrahydro-5-(1*H*-1,2,4-triazol-1yl-methyl)-furan-3-yl-methyl]-4-{4-[4-(benzyloxy)-phenyl]-1-piperazinyl]-phenyl}-2,4-dihydro-3(2*H*,4*H*)-1,2,4-triazolone,

2-[(5R,3R)-5-(2,4-difluorophenyl)-tetrahydro-5-(1<math>H-1,2,4-triazol-1yl-methyl)-furan-3-yl-methyl]-4-[4-(2,4-dichlorobenzyloxy)-phenyl]-2,4-dihydro-3(2H,4H)-1,2,4-triazolone,

- 5. A pharmaceutical composition comprising a therapeutically effective amount of a compound as defined in claim 1 or 4 and a pharmaceutically acceptable carrier or diluent.
- 6. A method of treating or preventing fungal infection in a mammal comprising administering to said mammal a therapeutically effective amount of a compound having the structure of Formula I

Formula I

and its pharmaceutically acceptable salts, enantiomers, diastereomers, Novides, prodrugs, metabolites, polymorphs, or pharmaceutically acceptable solvates,

wherein

Az is a five to seven membered heterocyclic ring having one to four heteroatoms selected from N, S, or O; the preferred heterocyclic ring is 1,2,4-triazol-1-yl;

Ar is a five to seven membered heterocyclic ring containing one to four heteroatoms selected from the group consisting of oxygen nitrogen and sulphur; phenyl or a substituted phenyl group having one to three substituents independently selected from halogen (e.g. chlorine, fluorine, bromine or iodine), nitro, cyano, lower(C_1 - C_4) alkyl, lower (C_1 - C_4) alkoxy or a perhalo lower (C_1 - C_4) alkyl, perhalo lower(C_1 - C_4) alkoxy; the preferred heterocyclic rings are thienyl and pyridyl;

R is H or methyl;

R₁ is selected from the group consisting of

wherein

X is selected from the group consisting of CH₂, O, S and SO₂;

R₂ is hydrogen or lower(C₁-C₄) alkyl;

A is hydrogen, lower(C_1 - C_4) alkyl, phenyl or phenyl substituted by one or more of groups independently selected from halogen (e.g. chlorine, fluorine, bromine or iodine atoms), nitro, cyano, hydroxy, lower(C_1 - C_4) alkyl, lower (C_1 - C_4) alkoxy or perhalo lower (C_1 - C_4) alkyl, perhalo lower (C_1 - C_4) alkoxy; substituted or unsubstituted five or six membered heterocyclyl ring systems containing one to four hetero atoms chosen from N, O and S, said heterocyclyl substituents being (C_1 - C_8) alkanoyl, lower (C_1 - C_4) alkyl, lower (C_1 - C_4) alkoxy carbonyl, N, N-di(lower alkyl)

 (C_1-C_4) amino carbonyl, aminothiocarbonyl, N-lower(C_1-C_4) alkyl aminothiocarbonyl, N,N-di(lower alkyl) (C_1-C_4) aminothiocarbonyl, lower (C_1-C_4) alkyl sulfonyl, phenyl substituted lower (C_1-C_4) alkyl sulfonyl, N-lower (C_1-C_4) alkylamino, N, N-di(lower alkyl) (C_1-C_4) amino, 1,3-imidazol-1-yl, 2-loweralkyl(C_1-C_4) sulfenyl-1,3-imidazol-1-yl, pyridinyl, thaizolyl, 1,2,4 triazol-4-yl or phenyl or phenyl substituted by one or more of groups independently selected from halogen (chlorine, fluorine, bromine or iodine), perhalo lower(C_1-C_4) alkyl, (C_2-C_8) alkanoyl, lower(C_1-C_4) alkyl, lower(C_1-C_4) alkyl substituted by one or more hydroxy group, lower(C_1-C_4) alkoxy, nitro, cyano, hydroxy, 1,2,4-triazolyl, 1,3-imidazolyl, 1,2,3,4-tetrazolyl.

- 7. A method of treating or preventing a fungal infection in a mammal comprising the step of administering to said mammal a therapeutically effective amount of the pharmaceutical composition according to claim 5.
- 8. A process for preparing a compound of the Formula I, its pharmaceutically acceptable salts, enantiomers, diastereomers, N-oxides, prodrugs, metabolites, polymorphs, or pharmaceutically acceptable solvates

wherein

Az is a five to seven membered heterocyclic ring having one to four heteroatoms selected from N, S, or O; the preferred heterocyclic ring is 1,2,4-triazol-1-yl;

Ar is a five to seven membered heterocyclic ring containing one to four heteroatoms selected from the group consisting of oxygen nitrogen and sulphur; phenyl or a substituted phenyl group having one to three substituents independently selected from halogen (e.g. chlorine, fluorine, bromine or iodine), nitro, cyano, lower(C₁-C₄) alkyl, lower (C₁-C₄) alkoxy or a perhalo lower (C₁-C₄) alkyl, perhalo lower(C₁-C₄) alkoxy; the preferred heterocyclic rings are thienyl and pyridyl;

R is H or methyl; R₁ is selected from the group consisting of

wherein

X is selected from the group consisting of CH2, O, S and SO2;

R₂ is hydrogen or lower(C₁-C₄) alkyl;

A is hydrogen, lower(C₁-C₄) alkyl, phenyl or phenyl substituted by one or more of groups independently selected from halogen (e.g. chlorine, fluorine, bromine or iodine atoms), nitro, cyano, hydroxy, lower(C1-C4) alkyl, lower(C₁-C₄) alkoxy or perhalo lower (C₁-C₄) alkyl, perhalo lower(C₁-C₄)alkoxy; substituted or unsubstituted five or six membered heterocyclyl ring systems containing one to four hetero atoms chosen from N, O and S, said heterocyclyl substituents being (C1-C8) alkanoyl, lower (C1-C4) alkyl, lower (C₁-C₄) alkoxy carbonyl, N, N-di(lower alkyl) (C₁-C₄) amino carbonyl, aminothiocarbonyl, N-lower(C₁-C₄) alkyl aminothiocarbonyl, N,N-di(lower alkyl) (C₁-C₄) aminothiocarbonyl, lower (C₁-C₄) alkyl sulfonyl, phenyl substituted lower (C1-C4) alkyl sulfonyl, N-lower(C1-C4) alkylamino, N, Namino, 1,3-imidazol-1-yl, 2-loweralkyl(C₁-C₄) di(lower alkyl) (C₁-C₄) sulfenyl-1,3-imidazol-1-yl, pyridinyl, thaizolyl, 1,2,4 triazol-4-yl or phenyl or phenyl substituted by one or more of groups independently selected from halogen (chlorine, fluorine, bromine or iodine), perhalo lower(C₁-C₄) alkyl, (C₂-C₈) alkanoyl, lower(C₁-C₄) alkyl, lower(C₁-C₄) alkyl substituted by one

or more hydroxy group, lower(C_1 - C_4) alkoxy, nitro, cyano, hydroxy, 1,2,4-triazolyl, 1,3-imidazolyl, 1,2,3,4-tetrazolyl;

which comprises reacting a compounds of Formula III with a compound of Formula IV as shown below, where all symbols are as defined above.

A process according to claim 8 for preparing a compound of the Formula II (Formula I, wherein Az is 1,2,4-triazol -1-lyl; R is H or CH₃; Ar is 2, 4-dihalo

Formula I

N N-A

substituted phenyl, Hal is Cl, F, Br or 1; and R1 is

9.

wherein A is the same as defined in claim 1, which comprises condensing 2,2,4 – trisubstituted tetrahydrofuran of the Formula V with 4 – substituted triazolone of Formula VI as shown below:

10. A process according to claim 9 for preparing a compound of Formula II, wherein A is represented by

$$-\sqrt{N-z}$$

Formula II

Z is a hydrogen, (C_1-C_8) alkanoyl, lower alkyl, (C_1-C_8) perhaloalkanoyl, or phenyl, phenyl substituted by one or more of groups independently selected from nitro, cyano, halogen (chlorine, fluorine bromine, iodine) perhalo lower(C_1-C_4) alkyl, perhalo lower(C_1-C_4) alkoxy; (C_2-C_8) alkanoyl, lower(C_1-C_4) alkyl, lower (C_1-C_4) alkyl substituted by one or more hydroxy group, lower(C_1-C_4) alkoxy, 1,3-imidazolyl, 1,2,4-triazolyl, 1,2,3,4-tetrazolyl, or OCH₂Y; wherein

Y is phenyl or phenyl substituted by one or more of groups independently selected from nitro, cyano, halo, perhalo lower alkyl, (C₂-C₈) alkanoyl lower

alkyl, hydroxy, lower alkyl substituted by one or more hydroxy group, lower alkoxy, 1,3-imidazolyl, 1,2,4-triazolyl or 1,2,3,4-tetrazolyl.

- 11. The process of claim 8 wherein the reaction of compound of formula III and formula IV is carried out in a suitable organic solvent wherein the solvent is selected from the group consisting of dimethylformamide, dimethyl sulfoxide, toluene, isopropyl alcohol, tetrahydrofuran, ethylene glycol, dimethyl ether, and mixtures thereof.
- 12. The process of claim 8 wherein the reaction of compound of formula III and formula IV is carried out in the presence a suitable base.
- 13. The process of claim 12 wherein the base is selected from the group consisting of sodium hydride, potassium carbonate, cesium carbonate, and sodium carbonate.